

## LETTERS TO THE EDITOR

## Phosphate intake and the CARE study

*To the Editor:* We read with great interest the Calcium Acetate Renagel Evaluation (CARE) study report [1]. Although this trial was designed according to the best standards, patients' weights were unexpectedly greater than 11% in the sevelamer group. Phosphate metabolism not only depends on dialytic clearance, but also on intake and absorption [2]. Thus, protein (based on 1.2 g protein/kg/day), and consequently phosphate (a nearly constant 1.3% of protein) intakes may have been greater in the sevelamer group by 10 g protein (e.g., 130 mg phosphate per day). It would be of great interest to provide normalized protein nitrogen appearance (nPNA) in order to rule out this confounding factor.

Similar to phosphate intake, we are left without indication upon vitamin D doses between groups. Indeed, combination of higher phosphate intake and vitamin D might have resulted in a larger phosphate absorption, and impacted on serum phosphate curve over time (Fig. 1A). Finally, the short duration of the trial might not have allowed for metabolic equilibrium to occur because, in the calcium acetate group, serum calcium seems to rise as soon as four weeks after the start (Fig. 2A), consequently followed by a rise in CaP product at week six, which could have counterbalanced the slower control of CaP product by sevelamer over time.

Hyperphosphatemia is present in more than 50% of maintenance dialysis patients, and there is a great variability in its care [3]. There is no need to underline the difficulty to conduct well-designed studies in this field, but our remark points out some limitations of the strong conclusions made by Qunibi et al.

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3. MARTIN CJ, REAMS SM: The renal dietitian's role in managing hyperphosphatemia and secondary hyperparathyroidism in dialysis patients: A national survey. *J Renal Nutr* 13:133–136, 2003

## Reply from the Authors

We thank Dr. Fouque for his thoughtful comments regarding the CARE study [1]. Indeed, baseline demographics showed a statistically significant difference in weight between the two treatment groups, such that the mean weight was 11% greater in the sevelamer-treated patients. However, analysis by repeated measures logistic regression showed that the difference in weight between the two groups had no effect on the primary “goal-attained” outcomes for serum phosphorus or calcium-phosphorus product. Moreover, three-day dietary histories were obtained on all patients at baseline, week four, and week eight to assess dietary intake of calcium and phosphorus, and there was not a statistically significant difference between the two groups at any time point during the study. Thus, we conclude that the difference in baseline weight between the two groups does not account for our finding that calcium acetate-treatment resulted in better control of serum phosphorus and calcium-phosphorus product than treatment with sevelamer hydrochloride. Unfortunately, we do not have data on normalized protein catabolic rate (nPCR) in our CARE study patients.

Prestudy use of injectable vitamin D preparations was similar in the two groups; 65% of the calcium acetate group versus 60% of the sevelamer group was treated with vitamin D ( $P = 0.64$ ). The study was designed such that the patient's prestudy dose of vitamin D was continued and maintained constant throughout the eight-week treatment period. Vitamin D doses were not modified in response to hypercalcemia or parathyroid hormone (PTH) levels.

Finally, the time-averaged serum calcium concentration was higher by 0.63 mg/dL in the calcium acetate group, whereas mean serum calcium levels did not change significantly from baseline values in the sevelamer group. Thus, the significant difference in calcium-phosphate product can only be explained by better control of serum phosphorus in the calcium acetate group. In this regard, because the magnitude of the change in serum phosphorus ( $C_{avg} = 1.08$  mg/dL over the 8-week study) is larger than the average change in serum calcium, the attained

serum phosphorus seems to be the most important variable in determining the observed difference in calcium-phosphorus product between the treatment groups.

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## Using the right MDRD equation

*To the Editor:* Estimating the prevalence of renal insufficiency in any patient population is of course a crucial issue. The earlier renal insufficiency is diagnosed, the best care is to be provided to the patient, especially in terms of slackening the progression of renal failure and adjusting drugs dosage when required. In their article, Garg *et al* [1] mentioned that they estimated the renal function of their patients using the Cockcroft-Gault and the Modification of Diet in Renal Disease Study (MDRD) formulas. They thus cited Cockcroft and Gault [2] and Levey *et al* [3] works in references. The authors further detailed the formulas they used in the **Appendix** of their article. It is important to remember that Levey *et al* tested in their work seven different formulas for estimating glomerular filtration rate. They concluded that among those equations, only one (equation 7) gave satisfactory results. This seventh equation is the one that should be used in other works when renal function is to be estimated with the MDRD equation. Unfortunately, the formula called MDRD formula in Garg's article is not the formula validated by Levey *et al* in the MDRD article.

MDRD equation for estimating glomerular filtration rate (GFR):

$$\begin{aligned} \text{GFR}(\text{mL}/\text{min}/1.73\text{m}^2) &= 170 \times [\text{P}_{\text{CR}}]^{-0.999} \\ &\times [\text{Age}]^{-0.176} \times [\text{SUN}]^{-0.170} \\ &\times [\text{Alb}]^{+0.318} \\ &\times 0.762 \text{ if patient is female} \\ &\times 1.180 \text{ if patient is black} \end{aligned}$$

with  $\text{P}_{\text{CR}}$  = serum creatinine concentration (mg/dL), Age = age of the patient (years), SUN = serum urea nitrogen (mg/dL), and Alb = serum albumin concentration (g/dL).

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## Reply from the Authors

We thank Launay-Vacher *et al* for their comment. Estimating glomerular filtration rate (GFR) in nursing home elderly is critical for drug dosing and end of life care, which may include dialysis. As we highlight in our paper, there are limitations to the use of both Cockcroft-Gault and Modification of Diet in Renal Disease Study (MDRD) formulas. The best methods of estimating GFR for patient care in this population remain to be clarified.

The abbreviated MDRD formula was used in our research study [1]. For transparency of reporting we included the formula in the **Appendix**. The abbreviated MDRD equation is used throughout Kidney Disease Outcomes Quality Initiative (K/DOQI) clinical practice guidelines [2], facilitating comparisons with our results. Levey *et al* suggest both MDRD equation 7 and the abbreviated MDRD formula correlate well with 125I-iothalamate GFR in middle-aged adults with kidney disease ( $R^2 = 0.90$  and  $0.89$ , respectively) [1]. Finally, the predictive validity of the abbreviated MDRD formula has been established—low GFR was a strong predictor of death and end-stage renal disease in a sample of 27,998 adults followed for 5 years [3]. Thus, we strongly disagree with Launay-Vacher *et al*'s assertion that MDRD equation 7 was the only valid formula to be used in our analyses.

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